Amendments to the Claims

Please amend the claims as follows:

- (Currently amended) An immunogenic composition comprising <u>at least one</u>
 Neisserial <u>autotransporter antigen and at least one</u> two or more different antigen[[s]],
 wherein the <u>at least one different antigen[[s]] are is</u> selected from <u>at least two of</u> the
 following categories:
- a) at least one Neisserial adhesin;
- b) at least one Neisserial autotransporter:
- b) at least one Neisserial toxin:
- c) at least one Neisserial Fe acquisition protein; or
- <u>d</u>)_at least one Neisserial membrane associated protein, preferably integral outer membrane protein.
- 2. (Currently amended) The immunogenic composition of claim I, wherein the antigens are at least one Neisserial autotransporter antigen is selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA; and the at least one different antigen is selected from at-least-two-of the following categories:
 - a) at least one Neisserial adhesin selected from the group consisting of FhaB, NspA, PilC, Hsf, Hap, MafA, MafB, Omp26, NMB0315, NMB0995, NMB1119 and NadA;
 - b) at least one Neisserial autotransporter-selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA;
 - e) b) at least one Neisserial toxin selected from the group consisting of FrpA, FrpC, FrpA/C, VapD, NM-ADPRT, and either or both of LPS immunotype L2 and LPS immunotype L3;
 - d) c) at least one Neisserial Fe acquisition protein selected from the group consisting of TbpA high, TbpA low, TbpB high, TbpB low, LbpA, LbpB, P2086, HpuA, HpuB, Lipo28, Sibp, FbpA, BfrA, BfrB, Bcp, NMB0964 and NMB0293; or

- e) d) at least one Neisserial membrane associated protein, preferably integral outer membrane protein selected from the group consisting of PilQ, OMP85, FhaC, NspA, TbpA(high), TbpA(low), LbpA, HpuB, TspA, TspB, TdfH, PorB, HimD, HisD, GNA1870, OstA, HlpA, MltA, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA and PldA.
- 3. (Previously presented) The immunogenic composition of claim 1 which is a subunit composition.
- 4. (Currently amended) The immunogenic composition of claim 3 emprising at least 2-antigens wherein the at least one Neisserial autotransporter antigen comprises the passenger domain of Hsf and the at least one different antigen is selected from the following list: FhaB, NspA, passenger domain of Hsf; passenger domain of Hap, surface exposed domain of OMP85, FrpA, FrpC, TbpB, LbpB, PldA, PilC, Lipo28 and either or both of LPS immunotype L2 and LPS immunotype L3.
- 5. (Previously presented) The immunogenic composition of claim 1 comprising an outer membrane vesicle preparation, wherein the antigens have been upregulated in the outer membrane vesicle.
- 6. (Currently amended) The immunogenic composition of claim 5 eomprising at least two antigens wherein the at least one Neisserial autotransporter antigen comprises Hsf and the at least one different antigen is selected from the following list-which have been upregulated in the outer membrane vesiele: NspA, Hsf, Hap, OMP85, AspA, HpuA, HpuB, TspA, TspB, FhaC, TbpA (high), TbpA (low), LbpA, TbpB, LbpB, PiIQ, NM-ADPRT, P2086, TdfH, PorB, MafA, MafB, HimD, HisD, GNA1870, OstA, HlpA, MltA and PldA; and optionally comprising either or both of LPS immunotype L2 and LPS immunotype L3.

wherein Hsf and the at least one different antigen are upregulated in the outer membrane vesicle.

- 7. (Previously presented) The immunogenic composition of claim 1 comprising a subunit composition having one or more of the antigens, and an outer membrane vesicle preparation having at least one antigen which has been upregulated in the outer membrane vesicle.
- 8. (Currently amended) The immunogenic composition of claim 7 comprising a subunit composition and an outer membrane vesicle preparation.
- wherein the subunit composition comprises at least one antigen selected from
 the following list: FhaB, NspA, passenger domain of Hsf, passenger domain of Hap,
 surface exposed domain of OMP85, FrpA, FrpC, TbpB, LbpB, PilC, Lipo28; and
 wherein the outer membrane vesicle preparation having at least one different
 antigen which has been upregulated in the outer membrane vesicle comprises at least
- one upregulated antigen selected from the following list, which is different from the at least one antigen in the subunit composition, which has been recombinantly upregulated in the outer membrane vesiele: NspA, Hsf, Hap, OMP85, AspA, HpuA, HpuB, TspA, TspB, FhaC, TbpA (high), TbpA (low), LbpA, TbpB, LbpB, PilQ, NM-ADPRT, P2086, TdfH, PorB, MafA, MafB, HimD, HisD, GNA 1870, OstA, HlpA, MItA and PldA: and
- ____optionally comprising either or both of LPS immunotype L2 and LPS immunotype L3, preferably within the outer membrane vesicle preparation.
- (Previously presented) The immunogenic composition of claim 5 comprising at least two different outer membrane vesicle preparations.
- 10. (Original) The immunogenic composition of claim 9 wherein one outer membrane vesicle preparation is immunotype L2 and one outer membrane vesicle preparation is immunotype L3.
- 11. (Currently amended) The immunogenic composition of elaims-claim I wherein the at least one Neisserial autotransporter antigen comprises. Hsf and the at least one different antigen comprises TbpA (high) are selected.

- 12. (Currently amended) The immunogenic composition of claim 1 wherein the at least one Neisserial autotransporter antigen comprises. Hsf and the at least one different antigen comprises. TbpA (low) are selected.
- 13. (Currently amended) The immunogenic composition of claim 11 <u>further comprising wherein-one</u> or more additional antigens <u>selected</u> from a list consisting of Hap, LbpB, OMP 85 and FrpA-are-further-selected.
- 14. (Previously presented) The immunogenic composition of claim 11 wherein LPS immunotype L2 is further selected.
- 15. (Previously presented) The immunogenic composition of claim 11 wherein LPS immunotype L3 is further selected.
- 16. (Currently amended) The immunogenic composition of claim 1-wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA; FhaB; and

is selected together with—at least one further antigen selected from the group consisting of: PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, Hsfr-LbpB, FrpA, FrpC, FrpA/C, NadA, OMP85, PldA, LbpA, TbpA (low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, Hap, IgA protease, AspA, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and either or both of LPS immunotype L2 and LPS immunotype L3.

17. (Currently amended) The immunogenic composition of claim 1 wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA:

NspA; and

is-selected-together-with-at least one further antigen selected from the group consisting of: FhaB, PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, Hsf, LbpB, FrpA, FrpC, FrpA/C, NadA; OMP85, PldA, LbpA, TbpA (low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, Hap, IgA protease, AspA, PilC, MltA, HimD, HisD, GNA1870, OstA, HlpA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and either or both of LPS immunotype L2 and LPS immunotype L3.

18. (Cancelled)

19. (Currently amended) The immunogenic composition of claim 1 wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA;

TbpA (low); and

is-selected together-with-at least one further antigen selected from the group consisting of: FhaB., PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, Hsf-LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, Hap, IgA-pretease, AspA, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and either or both of LPS immunotype L2 and LPS immunotype L3.

20. (Currently amended) The immunogenic composition of claim 1 wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA:

TbpA (high); and

is-selected-together-with-at least one further antigen selected from the group consisting of: FhaB, PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB

1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, Hsf; LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, <u>TbpA(low)</u>, TbpB(low), TbpB(high), HpuA, HpuB, Hap, IgA protease, AspA, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and either or both of LPS immunotype L2 and LPS immunotype L3.

21. (Currently amended) The immunogenic composition of claim 1 wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA;
LbbB: and

is selected together-with-at least one further antigen selected from the group consisting of: FhaB., PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, Hsf. FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpA(low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, Hap, IgA protease, AspA, PilQ, MIA, HimD, HisD, GNA1870, OstA, HlpA, NspA. TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and either or both of LPS immunotype L2 and LPS immunotype L3.

22. (Currently amended) The immunogenic composition of claim 1 wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA;
OMP85; and

is selected together-with-at least one further antigen selected from the group consisting of: FhaB_PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, Hsf, LpbB_FrpA, FrpC, FrpA/C, PldA, LbpA, TbpA(low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, Hap, IgA-protease, AspA, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA_TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315,

NMB1119, TdfH, PorB, NM-ADPRT, VapD and either or both of LPS immunotype L2 and LPS immunotype L3.

23-24. (Cancelled)

25. (Currently amended) The immunogenic composition of claim I wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf. Hap, IgA protease, AspA and NadA;

Frp A; and

is selected together-with at least one further antigen selected from the group consisting of: FhaB., PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bep, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB., FrpC, FrpA/C, OMP85., PldA, LbpA, <a href="TbpA(low)., <a href="TbpB(low)., <a href="TbpB(ligh)., <a href="TbpB(ligh).</

26. (Currently amended) The immunogenic composition of claim I wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA;

FrpC: and

is selected together with at least one further antigen selected from the group consisting of: Fhab., PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, Lobpe, FrpA, FrpA/C, OMP85, PldA, LbpA, TbpA(low), <a href="TbpB(low), <a href="TbpB(ligh), <a

27. (Currently amended) The immunogenic composition of claim 1 wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA;

LPS immunotype L2: and

is selected together with at least one further antigen selected from the group consisting of: Fhab. PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB.FrpA.FrpC, FrpA/C.OMP85, PldA, LbpA, <a href="TbpA(low), <a href="TbpB(high), <a href="TbbB(high), <a href="TbbB(high)</a

28. (Currently amended) The immunogenic composition of claim 1 wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA;

LPS immunotype L3; and

is selected together-with at least one further antigen selected from the group consisting of: Fhab., PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB.FrpA.FrpC.FrpA/C.OMP85, PidA, LbpA, TbpB(high), TbpB(high), HpuA, HpuB, Hga-Protease-AspA-PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspB, 72086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT_ and VapD and Lps immunotype-L2.

29. (Currently amended) The immunogenic composition of claim 1 wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA;

PilQ; and

is selected together with at least one further antigen selected from the group consisting of: FhaB. PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB

1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpA(low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, IgA-protease, AspA, MltA, HimD, HisD, GNA 1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, and VapD and either or both of LPS immunotype L2 and LPS immunotype L3.

30. (Currently amended) The immunogenic composition of claim 1 wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA;

HlpA; and

is selected together with at least one further antigen selected from the group consisting of: FhaB, PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bep, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpA(low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, IgA protease, AspA, PilO, MltA, HimD, HisD, GNA1870, OstA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, and-VapD and either or both of LPS immunotype L2 and LPS immunotype L3.

31. (Currently amended) The immunogenic composition of claim | wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf. Hap, IgA protease, AspA and NadA:

MltA: and

-is selected together with at least one further antigen selected from the group consisting of: FhaB_a PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bep, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpA(low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, IgA protease, AspA, PilO, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315,

NMB1119, TdfH, PorB, NM-ADPRT, and VapD and either or both of LPS immunotype L2 and LPS immunotype L3.

32. (Currently amended) The immunogenic composition of claim 1 wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA;
GNA1870; and

is selected together-with-at least one further antigen selected from the group consisting of: FhaB_PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpA(low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, IgA-protease, AspA, PilQ, MItA, HimD, HisD, OstA, HIpA, NspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, and-VapD and either or both of LPS immunotype L2 or LPS immunotype L3.

33. (Currently amended) The immunogenic composition of claim 1 wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA;
NM-ADPRT: and

is selected together with at least one further antigen selected from the group consisting of: Fhab., PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB.FrpA.FrpC, FrpA/C, OMP85, PldA, LbpA, <a href="TbpA(low), <a href="TbpA(high), <a href="TbpB(low), <a href="TbpB(high), <a href="TbbB(high), <a

34. (Currently amended) The immunogenic composition of claim 1 wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA;

MafA; and

is selected together with at least one further antigen selected from the group consisting of: FhaB, PilC, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpA(low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, IgA protease, AspA, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, and VapD and either or both of LPS immunotype L2 or LPS immunotype L3.

35. (Currently amended) The immunogenic composition of claim 1 wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf. Hap. IgA protease, AspA and NadA;
MafB: and

is selected together with at least one further antigen selected from the group consisting of: FhaB. PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpA(low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, IgA protease, AspA, PilQ, MItA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, and-VapD and either or both of LPS immunotype L2 or LPS immunotype L3.

36. (Currently amended) The immunogenic composition of claim 1 wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA;
NMB0315; and

is selected together with at least one further antigen selected from the group consisting of: FhaB, PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpA(low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, IgA protease, AspA, PilO, MItA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB1119, TdfH, PorB, NM-ADPRT, and VapD and either or both of LPS immunotype L2 or LPS immunotype L3.

37. (Currently amended) The immunogenic composition of claim 1 wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA;
NMB1119: and

is-selected together-with-at least one further antigen selected from the group consisting of: FhaB, PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bep, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpA(low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, IgA-protease, AspA, PilO, MItA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1H19, TdH, PorB, NM-ADPRT, and-VapD and either or both of LPS immunotype L3 or LPS immunotype L3.

38. (Currently amended) The immunogenic composition of claim 1 wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA;

HisD: and

is selected together-with-at least one further antigen selected from the group consisting of: FhaB, PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpA(low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, HgA protease, AspA, PilO, MltA, HimD, GNA1870, OstA, HlpA.

NSpA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, and VapD and either or both of LPS immunotype L2 or LPS immunotype L3.

39. (Currently amended) The immunogenic composition of claim 1 wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf. Hap, IgA protease, AspA and NadA;

LbpA; and

is selected together with at least one further antigen selected from the group consisting of: FhaB, PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, TbpA(low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, IgA-protease, AspA, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, and-VapD and either or both of LPS immunotype L2 or LPS immunotype L3.

40. (Currently amended) The immunogenic composition of claim 1 wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA;

NMB 0995; and

is selected together with at least one further antigen selected from the group consisting of: FhaB, PilC, MafA, MafB, Omp26, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpA(low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, IgA protease, AspA, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, and VapD and either or both of LPS immunotype L2 or LPS immunotype L3.

41. (Currently amended) The immunogenic composition of claim 1 wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA;
Lipo28: and

is selected together with at least one further antigen selected from the group consisting of: FhaB_PilC, MafA_MafB, Omp26, NMB0995, FhaC, FbpA, Bep, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB_FrpA_FrpC, FrpA/C, OMP85, PldA, LbpA_TbpA(low), TbpA (high), TbpB(low), TbpB(high), HpuA, HpuB, IgA protease, AspA, PilQ_MItA, HimD, HisD, GNA1870, OstA, HlpA_NspA, TspA, TspB, P2086, Sibp, NMB0964, NMB0293, NMB0315.

NMB1119, TdfH, PorB, NM-ADPRT, and-VapD and either or both of LPS immunotype L3 or LPS immunotype L3.

42. (Currently amended) The immunogenic composition of claim 1 wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf. Hap, IgA protease, AspA and NadA;
HimD; and

is selected together with at least one further antigen selected from the group consisting of: Fhab., PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB.FrpA.FrpC, FrpA/C.OMP85, PldA, LbpA(high), TbpB(low), TbpB(low), TbpB(high), HpuA, HpuB, HpaA. PilO, MILA, HisD, GNA1870, OstA, HlpA, NspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB1119, TdfH, PorB, NMB-ADPRT, and VapD and either or both of LPS immunotype L2 or LPS immunotype L3.

43. (Currently amended) The immunogenic composition of claim 1 wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA; NMB1313; and is selected together with at least one further antigen selected from the group consisting of: FhaB_PilC, MafA_MafB, Omp26, NMB0995, FhaC, FbpA, Bep, NMB 1124, NMB 1162, NMB 1220, NMB 1953, HtrA, LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpA(low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, IgA protease, AspA, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, and VapD and either or both of LPS immunotype L2 or LPS immunotype L3.

- 44. (Currently amended) The immunogenic composition of claim 1 wherein comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA; NMB1953; and
- is selected together with at least one further antigen selected from the group consisting of: Fhab., PilC, MafB, Fhab., FrpA, FrpA, FrpA, FrpA, TbpA(low), TbpB(low), <a href="TrpBB(low), DafA, DafA, DafA, NafA, MafA, <a href=
- 45. (Previously presented) The immunogenic composition of claim 5 wherein a host cell from which the outer membrane vesicle preparation is derived has been engineered so as to down-regulate the expression from one or more of lgtB or lgtE.
- 46. (Currently amended) The immunogenic composition of claim 5 wherein a host cell from which the outer membrane vesicle preparation is derived is unable to synthesize capsular polysaccharide and has preferably been engineered so as to down-regulate the expression from one or more of siaD, ctrA, ctrB, ctrC, ctrD, synA

(equivalent to synX and siaA) or synB (equivalent to siaB and synC (equivalent to siaC), preferably siaD.

- 47. (Currently amended) The immunogenic composition of claim 5 wherein a host cell from which the outer membrane vesicle preparation is derived has been engineered so as to down-regulate the expression of one or more of OpC, OpA or PorA, preferably PorA.
- 48. (Previously presented) The immunogenic composition of claim 5 wherein a host cell from which the outer membrane vesicle preparation is derived has been engineered so as to down-regulate the expression of FrpB.
- 49. (Currently amended) The immunogenic composition of claim 5 wherein a host cell from which the outer membrane vesicle preparation is derived has been engineered so as to down-regulate the expression from msbB and/or htrB, preferably msbB.
- 50. (Previously presented) The immunogenic composition of claim 5 wherein the outer membrane vesicle preparation contains LPS which is conjugated to an outer membrane protein (OMP).
- 51. (Currently amended) The immunogenic composition of claim 50 wherein LPS is conjugated (preferably intra-bleb-) to OMP in situ in the outer membrane vesicle preparation.
- 52. (Currently amended) The immunogenic composition of claim 1 comprising an antigen derived from *Neisseria meningitidis*, preferably-serogroup B.
- 53. (Previously presented) The immunogenic compositions of claim 1 comprising an antigen derived from *Neisseria gonorrhoeae*.

- 54. (Previously presented) The immunogenic composition of claim 1 wherein all neisserial antigens are derived from N.meningitidis.
- 55. (Previously presented) The immunogenic composition of claim | further comprising one or more bacterial capsular polysaccharides or oligosaccharides.
- 56. (Original) The immunogenic composition of claim 55 wherein the capsular polysaccharides or oligosaccharides are derived from bacteria selected from the group consisting of: Neisseria meningitidis serogroup A, C, Y and W-135, Haemophilus influenzae b, Streptococcus pneumoniae, Group A Streptococci, Group B Streptococci, Staphylococcus aureus and Staphylococcus epidermidis.
- 57. (Previously presented) The immunogenic composition of claim 55 wherein the capsular polysaccharide or oligosaccharide is conjugated to a protein.
- 58. (Previously presented) The immunogenic composition of claim 1 comprising an adjuvant.
- (Previously presented) The immunogenic composition of claim 58 comprising aluminium salts.
- $60. \mbox{ (Previously presented) The immunogenic composition of claim 58 comprising 3D-MPL. }$
- 61. (Previously presented) A vaccine comprising the immunogenic composition of claim 1 and a pharmaceutically acceptable carrier.
- 62. (Currently amended) A vaccine comprising one or more polynucleotide(s) encoding at least one Neisserial autotransporter protein and at least one two or more different protein[[s]] whose expression is driven by a eukaryotic promoter, wherein the at least one Neisserial autotransporter protein is selected from the group consisting

- of Hsf, Hap, IgA protease, AspA and NadA, and the at least one different protein[[s]] are is selected from at least two of the following categories:
 - a) at least one Neisserial adhesin selected from the group consisting of FhaB, NspA, PiIC, Hsf, Hap, MafA, MafB, Omp26, NMB0315, NMB0995, NMB1119 and NadA;
 - -at least one Neisserial autotransporter selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA;
 - at least one Neisserial toxin selected from the group consisting of FrpA,
 FrpC, FrpA/C, VapD and NM-ADPRT;
 - c) at least one Neisserial Fe acquisition protein selected from the group consisting of TbpA high, TbpA low, TbpB high, TbpB low, LbpA, LbpB, P2086, HpuA, HpuB, Lipo28, Sibp, FbpA, BfrA, BfrB, Bcp, NMB0964 and NMB0293; or
 - d) at least one Neisserial membrane associated protein, preferably integral outer membrane protein selected from the group consisting of PilQ, OMP85, FhaC, NspA, TbpA(high), TbpA(low), LbpA, HpuB, TspA, TspB, TdfH, PorB, HimD, HisD, GNA1870, OstA, HlpA, MitA, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA and PldA.
- 63. (Previously presented) A method for treatment or prevention of Neisserial disease comprising administering a protective dose of the vaccine of claim 61 to a host in need thereof.
- 64. (Original) The method of claim 63 in which *Neisseria meningitidis* infection is prevented or treated.
- 65. (Original) The method of claim 63 in which Neisseria gonorrhoeae infection is prevented or treated.

66-68. (Cancelled)

- 69. (Previously presented) A genetically engineered Neisserial strain from which the outer membrane vesicle preparation of claim 5 is derived.
- 70. (Previously presented) A method of making the immunogenic composition of claim 1 comprising a step of mixing together at least two antigens from Neisseria.
- 71. (Currently amended) A method of making the immunogenic composition of elaim-1 claim 5 comprising a step of isolating outer membrane vesicles from a Neisserial culture.
- 72. (Original) The method of claim 71 comprising a further step of combining at least two outer membrane vesicle preparations.
- 73. (Original) The method of claim 72 wherein at least one outer membrane vesicle preparation contains LPS of immunotype L2 and at least one outer membrane vesicle preparation contains LPS of immunotype L3.
- 74. (Previously presented) The method of claim 71 wherein the outer membrane vesicles are isolated by extracting with a concentration of DOC of 0 0.5%.
- 75. (Previously presented) The method of claim 74 wherein the outer membrane vesicles are isolated by extracting with a concentration of DOC of 0.02%-0.4%, 0.04%-0.3%, 0.06%-0.2%, 0.08%-0.15%.
- 76. (Previously presented) A method of making the vaccine of claim 61 comprising a step of combining the immunogenic composition with a pharmaceutically acceptable carrier.
- 77. (Original) A method of preparing an immune globulin for use in prevention or treatment of Neisserial infection comprising the steps of immunising a recipient with the vaccine of claim 61 and isolating immune globulin from the recipient.

- 78. (Original) An immune globulin prepared by the method of claim 77.
- 79. (Original) A pharmaceutical composition comprising the immune globulin of claim 78 and a pharmaceutically acceptable carrier.
- 80. (Original) A method for treatment or prevention of Neisserial infection comprising a step of administering to a patient an effective amount of the pharmaceutical preparation of claim 79.

81. (Cancelled)

- 82. (Previously presented) The immunogenic composition of claim 5, comprising a meningococcal bleb of immunotype L2 and a meningococcal bleb of immunotype L3.
- 83. (Original) The immunogenic composition of claim 82 wherein TbpA(high) is upregulated in one of the blebs.
- 84. (Previously presented) The immunogenic composition of claim 82 wherein TbpA(low) is upregulated in one of the blebs.
- 85. (Previously presented) The immunogenic composition of claim 82 wherein Hsf is upregulated in one of the blebs.
- 86. (Previously presented) The immunogenic composition of claim 82 wherein OMP85 is upregulated in one of the blebs.
- 87. (Currently amended) The immunogenic composition of claim 82 wherein the blebs are isolated from meningococcal strains incapable of making capsular polysaccharide, preferably-siaD*.

- 88. (Previously presented) The immunogenic composition of claim 82 wherein the L2 and/or L3 LPS oligosaccharide structures are truncated consistent with the blebs having been isolated from meningococcal strains that are lgtB.
- 89. (Currently amended) The <u>immunogenie immunogenie</u> composition of claim 82 wherein the blebs are isolated from meningococcal strains that have downregulated expression of msbB.
- 90. (Previously presented) The immunogenic composition of claim 82 wherein the L2 and/or L3 LPS oligosaccharide moieties are intra-bleb conjugated to outer-membrane proteins integral to the bleb.
- 91. (Previously presented) The immunogenic composition of claim 82 wherein the blebs are derived from meningococcal strains which have downregulated expression of one or more of: FrpB, PorA, Opa or Opc.
- (New) The immunogenic composition of claim 52 comprising a protein antigen derived from Neisseria meningitidis serogroup B.
- 93. (New) The immunogenic composition of claim 1 comprising at least one Neisserial autotransporter antigen selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA;

FrpA/C; and

at least one further antigen selected from the group consisting of: PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, OMP85, PldA, LbpA, TbpA (low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and either or both of LPS immunotype L2 and LPS immunotype L3.

94. (New) The immunogenic composition of claim 16 comprising Hsf;

FhaB; and

at least one further antigen selected from the group consisting of: PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpA (low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, Hap, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and either or both of LPS immunotype L2 and LPS immunotype L3.

95. (New) The immunogenic composition of claim 17 comprising Hsf;

NspA; and

at least one further antigen selected from the group consisting of: FhaB, PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, Hsf, LbpB, FrpA, FrpC, FrpA/C, NadA, OMP85, PldA, LbpA, TbpA (low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, Hap, IgA protease, AspA, Hap, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and either or both of LPS immunotype L2 and LPS immunotype L3.

96. (New) The immunogenic composition of claim 20 comprising Hsf;

TbpA (high); and

at least one further antigen selected from the group consisting of: FhaB, PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bep, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpB(low), TbpB(high), HpuA, HpuB, Hap, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293,

NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and either or both of LPS immunotype L2 and LPS immunotype L3.

97. (New) The immunogenic composition of claim 21 comprising Hsf;

LbpB; and

at least one further antigen selected from the group consisting of: FhaB, PiIC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpA(low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, Hap, PiIQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and either or both of LPS immunotype L2 and LPS immunotype L3.

98. (New) The immunogenic composition of claim 22 comprising Hsf;

OMP85; and

at least one further antigen selected from the group consisting of: FhaB, PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LpbB, FrpA, FrpC, FrpA/C, PldA, LbpA, TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, Hap, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and either or both of LPS immunotype L2 and LPS immunotype L3.

99. (New) The immunogenic composition of claim 27 comprising Hsf;

LPS immunotype L2; and

at least one further antigen selected from the group consisting of: FhaB, PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA,

TbpA(low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, Hap, PilQ, MItA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and LPS immunotype L3.

100. (New) The immunogenic composition of claim 28 comprising Hsf;

LPS immunotype L3; and

at least one further antigen selected from the group consisting of: FhaB, PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, PldA, LbpA, LbpB, FrpA, FrpC, FrpA/C, OMP85, TbpA(low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, Hap, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and LPS immunotype L2.

101. (New) The immunogenic composition of claim 32 comprising Hsf;

GNA1870; and

at least one further antigen selected from the group consisting of: FhaB, PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bep, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpA(low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, PilQ, MltA, HimD, HisD, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and either or both of LPS immunotype L2 or LPS immunotype L3.

102. (New) The immunogenic composition of claim 41 comprising Hsf;
Lipo28; and

at least one further antigen selected from the group consisting of: FhaB, PilC, MafA, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpA(low), TbpA (high), TbpB(low), TbpB(high), HpuA, HpuB, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Sibp, NMB0964, NMB0293, NMB0315,TdfH, PorB, NM-ADPRT, VapD, and either or both of LPS immunotype L2 or LPS immunotype L3.

103. (New) The immunogenic composition of claim 93 comprising Hsf;

FrpA/C; and

at least one further antigen selected from the group consisting of: PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, OMP85, PldA, LbpA, TbpA (low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, Hap, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and either or both of LPS immunotype L2 and LPS immunotype L3.

104. (New) The immunogenic composition of claim 16 comprising NadA;

FhaB; and

at least one further antigen selected from the group consisting of: PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpA (low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, Hap, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and either or both of LPS immunotype L2 and LPS immunotype L3.

105. (New) The immunogenic composition of claim 17 comprising

NadA:

NspA; and

at least one further antigen selected from the group consisting of: FhaB, PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, Hsf, LbpB, FrpA, FrpC, FrpA/C, NadA, OMP85, PldA, LbpA, TbpA (low), TbpA(high), TbpB(high), HpuA, HpuB, Hap, IgA protease, AspA, Hap, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and either or both of LPS immunotype L2 and LPS immunotype L3.

106. (New) The immunogenic composition of claim 20 comprising NadA;

TbpA (high); and

at least one further antigen selected from the group consisting of: FhaB, PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpB(low), TbpB(high), HpuA, HpuB, Hap, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and either or both of LPS immunotype L2 and LPS immunotype L3.

107. (New) The immunogenic composition of claim 21 comprising NadA:

LbpB; and

at least one further antigen selected from the group consisting of: FhaB, PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpA(low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, AspA, Hap, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28,

Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and either or both of LPS immunotype L2 and LPS immunotype L3.

108. (New) The immunogenic composition of claim 22 comprising NadA;

OMP85; and

at least one further antigen selected from the group consisting of: FhaB, PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LpbB, FrpA, FrpC, FrpA/C, PldA, LbpA, TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, Hap, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and either or both of LPS immunotype L2 and LPS immunotype L3.

109. (New) The immunogenic composition of claim 27 comprising NadA;

LPS immunotype L2; and

at least one further antigen selected from the group consisting of: FhaB, PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpA(low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, Hap, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and LPS immunotype L3.

110. (New) The immunogenic composition of claim 28 comprising NadA;

LPS immunotype L3; and

at least one further antigen selected from the group consisting of: FhaB, PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, PldA, LbpA, LbpB, FrpA/C, OMP85, TbpA(high).

TbpB(low), TbpB(high), HpuA, HpuB, Hap, PilQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and LPS immunotype L2.

111. (New) The immunogenic composition of claim 32 comprising NadA;

GNA1870; and

at least one further antigen selected from the group consisting of: FhaB, PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpA(low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, PilQ, MltA, HimD, HisD, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and either or both of LPS immunotype L2 or LPS immunotype L3.

112. (New) The immunogenic composition of claim 41 comprising NadA;

Lipo28; and

at least one further antigen selected from the group consisting of: FhaB, PiIC, MafA, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, FrpA/C, OMP85, PldA, LbpA, TbpA(low), TbpA (high), TbpB(low), TbpB(high), HpuA, HpuB, PiIQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Sibp, NMB0964, NMB0293, NMB0315,TdfH, PorB, NM-ADPRT, VapD, and either or both of LPS immunotype L3 or LPS immunotype L3.

113. (New) The immunogenic composition of claim 93 comprising NadA;

FrpA/C; and

at least one further antigen selected from the group consisting of : PilC, MafA, MafB, Omp26, NMB0995, FhaC, FbpA, Bcp, NMB 1124, NMB 1162, NMB 1220, NMB

1313, NMB 1953, HtrA, LbpB, FrpA, FrpC, OMP85, PIdA, LbpA, TbpA (low), TbpA(high), TbpB(low), TbpB(high), HpuA, HpuB, Hap, PiQ, MltA, HimD, HisD, GNA1870, OstA, HlpA, NspA, TspA, TspB, P2086, Lipo28, Sibp, NMB0964, NMB0293, NMB0315, NMB1119, TdfH, PorB, NM-ADPRT, VapD and either or both of LPS immunotype L2 and LPS immunotype L3.

114. (New) The immunogenic composition of Claim 5 wherein the antigens have been upregulated in the outer membrane vesicle by growth of a parental strain of Neisseria under iron limitation conditions.

115. (New) The immunogenic composition of Claim 7 wherein the at least one antigen upregulated in the outer membrane vesicle has been upregulated by growth of a parental strain of Neisseria under iron limitation conditions.